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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,546	10/06/2001	Stephen M. Strittmatter	A116 US	4440

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EXAMINER	
NICHOLS, CHRISTOPHER J	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/972,546	STRITTMATTER ET AL.	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *11-21 and 23-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I (claims 1-10 and 22) in Paper No. 11 (27 March 2003) drawn to SEQ ID NO: 2, vectors, and host cells comprising same is acknowledged. Claims 11-21 and 23-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11 (27 March 2003).

Information Disclosure Statement

2. The information disclosure statement filed 26 February 2002 (Paper No. 9) fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (pp. 108 line 13). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

4. Claims **1-10** and **22** are objected to because of the following informalities: recite non-elected subject matter. Appropriate correction is required.

5. Claim **5** is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The specification asserts that SEQ ID NO: 2 encodes the isoform hNgR2, while claim 5 is drawn to isoforms hNgR3 and mNgR3.

6. Claim **22** is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to previous claims in the alternative only. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims **1-10** and **22** are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial, and credible asserted utility. The specification discloses the isolated nucleic acid molecule SEQ ID NO: 2. The specification asserts that the isolate nucleic acid molecule SEQ ID NO: 2 encodes a novel Nogo receptor, specifically novel human Nogo receptor 2 (hNgR2). Concerning the Nogo receptor family, Pignot *et al.* (2003) "Characterization of two novel proteins, NgRH1 and NgRH2, structurally and biochemically homologous to the Nogo-66 receptor." Journal of Neurochemistry **85**(3): 717-728 teaches that Nogo-66 (a protein to which SEQ ID NO: 2 shares homology) is a member of the which is a member of the leucine-rich repeat (LRR) family (pp. 718). The LRR motif is found in a functionally and evolutionarly diverse group of proteins including but not limited to signal-transduction receptors and adhesion molecules (pp. 718). On the LRR family, Kobe and Kajava (December 2001) "The leucine-rich repeat as a protein recognition motif." Current Opinion Structural Biology **11**(6): 725-32 teach that leucine rich repeats (LRR) are a structural motif that are generally 20-29 amino acids long and contain a conserved 11-residue segment with the consensus sequence "LxxLxLxx$^{N}/_{C}$xL" wherein "x" can be any amino acid and L positions can be valine, isoleucine, or phenylalanine although generally are leucine (pp. 725). Known LRR containing proteins fall into one of seven subfamilies: RI-like, SDS22-like, cysteine-containing, Bacterial, Typical, Plant-specific, and TpLRR (Table 1 and 2). These known seven subfamilies cover a wide range of proteins such as

GTPase-activating protein RNA 1p, splicesomal protein U2A', Rab geranylgeranyltransferase, internalin B, dynein light chain 1, and TAP, Skp2, and YopM. LRR proteins are found in mammals, plants, and bacteria (pp. 725). The specification does not disclose any data for any activity for the polypeptide encoded by SEQ ID NO: 2. There are no working examples. There are no well-established utilities for newly discovered biological molecules. However, the specification contains several assertions of utilities. Each will be discussed in turn.

a. *The isolated nucleic acid molecule SEQ ID NO: 2 encodes a novel human Nogo receptor (hNgR2):* The Applicant's assertion that SEQ ID NO: 2 (hNgR2) is a LRR protein which is an Nogo receptor is credible because it shares sequence homology with known LRR Nogo receptor including but not limited to Fournier *et al.* (18 January 2001) "Identification of a receptor mediating Nogo-66 inhibition of axonal regeneration." Nature **409**(6818): 341-346, where SEQ ID NO: 2 shares 36.3% sequence homology with Nogo-66. It is noted that Fournier *et al.* performed functional assays to confirm their identification of Nogo-66 (Figure 6). However, this assertion is not specific, as the art recognizes a number of Nogo receptor members of the LRR family nor is it substantial. Firstly, it is not clear from the specification or the claims to which Nogo receptor members of the LRR family is claimed. For instance, Khodadoust US 2002/0025554 A1 (28 February 2002) discloses 41 known proteins which contain LRRs (Fig. 5). These proteins include proteins from mammals (bovine, murine, human, procine), *Drosophila*, yeast (*S. cerevisise*, *S. pombe*) and bacteria (*L. monocytogenes* and *Y. pestis*). Secondly, Pignot *et al.* (2003) "Characterization of two novel proteins, NgRH1 and NgRH2, structurally and biochemically homologous to the Nogo-66 receptor." Journal of

Neurochemistry **85**(3): 717-728 discloses five known Nogo isoforms, Nogo-A, Nogo-B, Nogo-C, (Nogo-66), NgRH1, and NgRH2 (pp. 717-718). Pignot *et al.* found that NgRH1 and NgRH2 share 45% and 48% homology to Nogo-66 and they share 52% homology with one another (pp. 720, Figure 1). Thus it is not clear if 36.3% is sufficient to firmly establish SEQ ID NO: 2 as a true member of the Nogo family in the absence of functional data. Thus the specification's assertion that SEQ ID NO: 2 is a novel Nogo receptor is not a substantial assertion of utility, since significant further research would be required of the skilled artisan to determine what SEQ ID NO: 2's properties are.

b. *The isolated nucleic acid molecule SEQ ID NO: 2 encodes a polypeptide which has Nogo receptor biological activity:* The specification asserts that SEQ ID NO: 2 is a Nogo receptor (with LRR motifs), which based on its structural similarity to prior art of Nogo receptors that have been characterized. While this assertion is credible it is neither specific nor substantial. It is not specific because this assertion would not have been accepted by one skilled in the art because the art establishes that Nogo receptors, while structurally similar, are functionally diverse. It is not substantial because of the lack of a working example of Nogo receptor functional activity. The art teaches that using known and functionally established clones of LRRs can be related to genes of varying sequence homology, with or without LRRs. The assertion that SEQ ID NO: 2 is a LRR is not substantial because the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For instance, Andrade *et al.* (May-June 2001) "Protein Repeats: Structures, Functions, and Evolution." Journal of Structural Biology **134**(2-3): 117-131 teaches that protein repeats fall into six

major repeat families including LRR and several other lesser known repeat families (Table II and Table III). Andrade *et al.* also teaches that using sequence analysis is fraught with errors due to the varying number and length of repeats even with families. Also, repeats motifs, again within a single family, usually exist in noninteger multiples and their boundaries do not always coincide (pp. 117-119). Thus one must be cautious in their use of sequence homology to assign a structure and function to a protein on sequence alone. Sequence homology is not a reliable as the sole basis upon which to establish biological activity. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remarks that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of

function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. In any case, the art clearly shows that structural similarity of different LRRs is not predictive of expression patterns or functional similarity. For instance, Li *et al.* (15 November 1995) "The Genetic Defect in Two Well-Studied Cases of Bernard-Soulier Syndrome: A Point Mutation in the Fifth Leucine-Rich Repeat of Platelet Glycoprotein Ibα." Blood **86**(10): 3805-3814 teaches that a single substitution of a Leucine for Proline at position 129 does not affect transcription but does prevent surface expression of the receptor causing Bernard-Soulier syndrome (Fig. 3-9). Thus even a single change in a LRR protein can have dramatic effects. Therefore, the specification's assertion that SEQ ID NO: 2 encodes a polypeptide with LRR activity is not a substantial assertion of utility, since significant further research would be required of the skilled artisan to determine what those activities are due the differences in sequence.

c. *The isolated nucleic acid molecule (SEQ ID NO: 2) may be useful in diagnosis and therapy*: Neither the specification nor the art discloses any convincing evidence to show that SEQ ID NO: 2 has any relation or involvement in a known disease or disorder. Due to the large range of expression levels, the enormous variability within species and

tissues in expression level, the lack of controls, a skilled artisan would have had to experiment significantly to identify and characterize any presumed use or role in a particular disease/disorder and the subsequent therapy for SEQ ID NO: 2. Therefore, the asserted utility is not substantial.

d. *The isolated nucleic acid molecule (SEQ ID NO: 2) may be useful as a probe or primer:* The specification asserts that SEQ ID NO: 2 is useful as probes to detect genes or variants thereof, to identify potential genetic disorders, or to regulate expression of SEQ ID NO: 2. This asserted utility is credible, but is neither substantial nor specific. Since there is no substantial utility for the polypeptide, there is also no substantial utility for the probes to identify SEQ ID NO: 2 in tissues or biological samples. Wang *et al.* (1 July 2002) "Localization of Nogo-A and Nogo-66 Receptor Proteins at Sites of Axon-Myelin and Synaptic Contact." The Journal of Neuroscience **22**(13): 5505-5515 teaches that two related proteins, Nogo-A and NogoR are distributed throughout the adult mouse CNS including but not limited to the cerebral cortex, hippocampus, amydgdala, thalamus, corpus callosum, caudate-putamen, substantia nigra, cerebellum, and spinal cord in varying amounts (Table 1). Thus related proteins have a wide distribution pattern and it would take significant further research to determine if the instantly claimed novel Nogo receptor could be used as probes for particular diseases, since no nexus between a disease state and an alteration in SEQ ID NO: 2 expression levels or form (i.e., mutations) has been disclosed in the specification. Also, all polynucleotides can be used as "probes" to detect genes, thus the asserted utility is not specific.

e. *The isolated nucleic acid molecule (SEQ ID NO: 2) can be used to make polypeptides for analysis, characterization, or therapeutic uses:* This asserted utility is neither substantial nor specific. In recombinately expressing a polypeptide, the polynucleotide is transfected into a host cell and then the protein is recovered. However, the instant specification does not disclose any known function for the claimed polypeptide or any disease state, toxin, or poison associated with SEQ ID NO: 2. In addition, this utility assertion is not specific as it can be applied to any given polynucleotide. Therefore, it is not clear how the skilled artisan would use a polypeptide manufactured by this method, for analysis, characterization, or therapeutic uses. Since significant further research would be required to determine how to use the identified polynucleotide, the asserted utility is not substantial.

f. *The isolated nucleic acid molecule (SEQ ID NO: 2) is useful to make vectors and transformed host cells:* This asserted utility would only be substantial if the encoded polypeptide has a substantial utility. Otherwise, significant further research would be required of the skilled artisan to use the claimed nucleic acid molecules to make vectors and transformed host cells, since it is unclear when it would be desirable to use the vectors and/or transformed host cells.

g. *The isolated nucleic acid molecule (SEQ ID NO: 2) is useful for making transgenic animals:* No phenotype has been disclosed for such transgenic animals. In the absence of such disclosure, the skilled artisan would have to experiment significantly in order to determine how the transgenic animals could be used. Therefore, the asserted utility is not substantial.

h. *The isolated nucleic acid molecule (SEQ ID NO: 2) is useful to design antisense molecules:* This asserted utility would only be substantial if the encoded polypeptide has a substantial utility. Otherwise, significant further research would be required of the skilled artisan to use the claimed nucleic acid molecules to make antisense molecules, since it is unclear when it would be desirable to use the antisense molecules.

i. *The isolated nucleic acid molecule (SEQ ID NO: 2) is useful to make ribozymes and PNA moieties:* This asserted utility would only be substantial if the encoded polypeptide has a substantial utility. Otherwise, significant further research would be required of the skilled artisan to use the claimed nucleic acid molecules to make ribozymes and PNA moieties, since it is unclear when it would be desirable to use the ribozymes or PNA moieties.

j. *The isolated nucleic acid molecule (SEQ ID NO: 2) can be used to in screening assays as a probe:* The specification asserts that SEQ ID NO: 2 is useful as probes to detect genes or variants thereof, to identify potential genetic disorders, or to regulate expression of SEQ ID NO: 2. This asserted utility is credible, but is neither substantial nor specific. Since there is no substantial utility for the polypeptide, there is also no substantial utility for the probes to identify SEQ ID NO: 2 in tissues or biological samples. Hunt *et al.* (August 2002) "Nogo Receptor mRNA Expression in Intact and Regenerating CNS Neurons." Molecular and Cellular Neuroscience **20**(4): 537-552 teaches that using a probe from a known Nogo receptor (Nogo-66) yielded 23 different mRNA transcripts that were positive for a Nogo-66 sequence probe (Table 1). Therefore, using a sequence probe from known protein can yield numerous related and unrelated

mRNA transcripts. It would take significant further research to determine if the instantly claimed novel Nogo receptor could be used as probes for particular diseases, since no nexus between a disease state and an alteration in SEQ ID NO: 2 expression levels or form (i.e., mutations) has been disclosed in the specification. Also, all polypeptides can be used as "probes" to detect the genes encoding them, thus the asserted utility is not specific.

k. *The isolated nucleic acid molecule (SEQ ID NO: 2) can be used to identify ligands and screening assays*: *SEQ ID NO: 2 can be used in assays for drug screening to identify compounds that bind, modulate the activity of, alter the expression of SEQ ID NO: 2, or identify disease/disorder related modulators:* This asserted utility is not substantial. In such assays, compounds are screened for their ability to up-regulate or down-regulate activity of SEQ ID NO: 2. Compounds that have on or the other activity are then labeled as potential drugs. However, the instant specification does not disclose any specific disease state wherein there is a change in SEQ ID NO: 2 expression levels or forms (i.e., mutations). Therefore, it is not clear how the skilled artisan would use a potential drug identified by this method. Since significant further research would be required to determine how to use the identified potential drugs, the asserted utility is not substantial. This asserted utility is also not specific, since any protein can be used in such assays.

l. *The isolated nucleic acid molecule (SEQ ID NO: 2) can be used to make a pharmaceutical composition (such as with gene therapy):* Neither the specification nor the art discloses any convincing evidence to show that SEQ ID NO: 2 has any relation or

involvement in a known disease or disorder. Due to the large range of expression levels, the enormous variability within species and tissues in expression level, the lack of controls, a skilled artisan would have had to experiment significantly to identify and characterize any presumed use or role in a particular disease/disorder and the subsequent therapy for SEQ ID NO: 2. Therefore, the asserted utility is not substantial.

m. *The isolated nucleic acid molecule (SEQ ID NO: 2) is useful for pharmacogenomics:* This asserted utility would only be substantial if the encoded polypeptide had a substantial utility. Otherwise, significant further research would be required of the skilled artisan to use the claimed nucleic acid molecules in pharmocogenomics, since it is unclear when it would be desirable to use the SEQ ID NO: 2 without known diseases, disorders, allergies, or ailments associated with it.

n. *The isolated nucleic acid molecule (SEQ ID NO: 2) is useful for monitoring clinical efficacy:* This asserted utility would only be substantial if the encoded polypeptide had a substantial utility. Otherwise, significant further research would be required of the skilled artisan to use the claimed nucleic acid molecules in a clinical study, since it is unclear when it would be desirable to use the SEQ ID NO: 2 without known diseases, disorders, allergies, or ailments associated with it.

8. Therefore, in the absence of a well-established utility, and the absence of a specific, substantial and credible asserted utility, the claimed invention lacks patentable utility under 35 U.S.C. § 101.

If Applicant can submit evidence (in the form of a declaration under 37 CFR 1.132 or post-filing date publications) supporting the specification's assertion that SEQ ID NO: 2 has a specific function similar to a known human Nogo receptor, wherein the specific function was predicted by the specification as originally filed, such would be viewed favorably as evidence of patentable utility.

9. Claims **1-10** and **22** are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore regarding variants and fragments of **SEQ ID NO: 2** polypeptides, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to

determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1): 34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427). Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

10. Claims **1-10** and **22** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not contain a written description of variants and fragments of the claimed peptide-transmitter-like receptor polypeptide.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of **SEQ ID NO: 2**, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in **SEQ ID NO: 2**, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Summary

11. Claims **1-10** and **22** are hereby rejected.

12. The following was found by the Examiner during the art search for the instant Application and is here made of note:

a. WO 03/018631 A2 (6 March 2003) Barske *et al.*

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher James Nichols, Ph.D. whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, Ph.D. can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elyabeth C. Kemmerer

CJN
May 27, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER